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Root-cause analyses of missed opportunities for the diagnosis of colorectal cancer in patients with inflammatory bowel disease

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Summary

Background: Colonoscopic surveillance in patients with inflammatory bowel disease (IBD) leads to earlier detection of colorectal cancer (CRC) and reduces CRC-associated mortality. However, it is limited by poor adherence in practice.

Aim: To identify missed opportunities to detect IBD-associated CRC at our hospital

Methods: We undertook root-cause analyses to identify patients with missed opportunities to diagnose IBD-associated CRC. We matched patients with IBD-associated CRC to patients with CRC in the general population to identify differences in staging at diagnosis and clinical outcomes.

Results: Compared with the general population, patients with IBD were at increased risk of developing CRC (odds ratio 2.7 [95% CI 1.6–3.9], $P < 0.001$). The mean incidence of IBD-associated CRC between 1998 and 2019 was 165.4 (IQR 130.4–199.4) per 100 000 patients and has not changed over the last 20 years. Seventy-eight patients had IBD-associated CRC. Forty-two (54%) patients were eligible for CRC surveillance: 12% (5/42) and 10% (4/42) patients were diagnosed with CRC at an appropriately timed or overdue surveillance colonoscopy, respectively. Interval cancers occurred in 14% (6/42) of patients; 64% (27/42) of patients had a missed opportunity for colonoscopic surveillance where root-cause analyses demonstrated that 10/27 (37%) patients known to secondary care had not been offered surveillance. Four (15%) patients had a delayed diagnosis of CRC due to failure to account for previous colonoscopic findings. Seventeen (63%) patients were managed by primary care including seven patients discharged from secondary care without a surveillance plan. Matched case-control analysis did not show significant differences in cancer staging or 10-year survival outcomes.

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Conclusion: The incidence of IBD-associated CRC has remained static. Two-thirds of patients eligible for colonoscopic surveillance had missed opportunities to diagnose CRC. Surveillance programmes without comprehensive and fully integrated recall systems across primary and secondary care are set to fail.

1 | INTRODUCTION

Colonoscopic surveillance leads to the earlier detection of colorectal cancer (CRC) in patients with inflammatory bowel disease (IBD) and may reduce CRC-associated mortality.¹⁻⁴ International guidelines recommend that surveillance programs begin 8-10 years after diagnosis of IBD in all but those patients whose disease is limited to the ileum or rectum.⁵⁻⁷ Thereafter, the surveillance interval is determined by the adequacy and endoscopic and/or histological findings of the previous colonoscopy. However, the effectiveness of colonoscopic surveillance in routine practice has been questioned because of poor adherence to surveillance protocols outside of clinical trials.^{8,9}

Root-cause analyses were developed originally to recognise factors that cause variation in performance in high-risk organisations including aviation and nuclear power.^{10,11} In healthcare, they have been applied to complex systems to understand why adverse outcomes occur. To prevent CRC, at-risk patients should be enrolled into surveillance programs so that pre-malignant lesions can be detected and completely resected. Because CRC can be diagnosed shortly after a normal colonoscopy, the World Endoscopy Organisation has constructed a root-cause analysis framework to identify why, so-called post-colonoscopy cancers, occur.^{12,13} Using this tool to report factors linked to post-colonoscopy cancers in a mixed cohort of surveillance patients, the authors from an academic endoscopy centre in the UK, recommend extra vigilance in patients with IBD.¹³

We sought to define the proportion of patients diagnosed with an IBD-associated CRC who had had a missed opportunity for colorectal surveillance and whether this influenced stage at diagnosis of CRC or survival outcomes.

2 | METHODS

2.1 | Study design and clinical setting

Using the World Endoscopy Organisation framework, we undertook a root-cause analysis to identify missed opportunities to diagnose IBD-associated CRC. We then designed a case-control matching study to define CRC survival outcomes in patients with IBD compared to the general population.

The Royal Devon & Exeter NHS Trust is an acute hospital that serves 48 general practices and about 400 000 people in North, East and West Devon. We estimate that the prevalence of ulcerative colitis (UC) and Crohn's disease is 479 per 100 000 and 266 per 100 000 respectively.¹⁴

2.2 | Case identification and data acquisition

Structured CRC outcome data have been collected prospectively since 1998 (Dendrite Clinical Systems LTD). We cross-referenced all patients diagnosed with CRC between March 1998 and March 2019 with our IBD database (Infoflex, Chameleon Information Management Services) to identify patients with IBD-associated CRCs. Patients were excluded from the study if they were diagnosed with IBD after the diagnosis of CRC.

Two researchers (C.G and D.C) retrieved data from paper and electronic medical records and our endoscopy (Unisoft GI reporting tool, HD Clinical) and histology databases (Swift Integrated Healthcare Solutions DXC Technology Company). Variables recorded included patient demographics (age, sex, ethnicity, smoking status, comorbidities according to the Charlson Comorbidity Index), IBD history (disease duration and phenotype according to the Montreal classification previous and concomitant medical therapies, IBD-related surgeries and treating physician) and colonoscopic surveillance history (family history of CRC, primary sclerosing cholangitis, endoscopic/histological findings at the last test including quality of bowel preparation, completion, disease activity, dysplasia, strictures and post-inflammatory polyps).^{15,16} Data regarding tumour location, stage at diagnosis and survival outcomes were also obtained from a CRC disease database.

2.3 | Root-cause analysis

Each pseudonymised surveillance history was reviewed by four gastroenterologists and we applied the following root-cause analysis steps to define the proportion of patients who had a missed opportunity for surveillance. Discrepancies were resolved by further review of source documents.

Step 1: Did the patient meet contemporaneous criteria for CRC surveillance of their IBD at the time their CRC was diagnosed?

If no, the patient was removed from our root-cause analysis; if yes, we proceeded to step 2.

Step 2: Considering the patient's age, comorbidities and personal preferences was surveillance indicated/appropriate?

If no, the patient was removed from our root-cause analysis; if yes, we proceeded to step 3.

Step 3: Was the CRC diagnosed at a surveillance colonoscopy?

If no, proceed to step 5; if yes, proceed to step 4.

Step 4: Was the surveillance colonoscopy which diagnosed the CRC performed within the correct time interval (no later than 3

months after the recommended interval according to contemporaneous IBD surveillance guidelines)?

If yes, the case was categorised as 'A': CRC diagnosed at timely surveillance colonoscopy.

If no, the case was categorised as 'B': CRC diagnosed at overdue surveillance colonoscopy.

Step 5: Had the patient been receiving optimal surveillance, according to contemporaneous guidelines, prior to the diagnosis of CRC?

If yes, the case was categorised as 'C': interval cancer.

If no, the case was categorised as 'D': missed opportunity to diagnose CRC.

2.4 | Case-control analysis to define survival outcomes of patients with IBD-associated CRC

We compared CRC stage at diagnosis in patients with and without IBD. Patients with recurrent CRC and those referred from outside our catchment area were excluded to mitigate selection and tertiary referral bias. We then matched each case of IBD-associated CRC to four control patients, with CRC but not IBD, for age, sex, tumour location and stage.¹⁷ We report all-cause mortality in cases and controls subsequently stratified by the outcome of our root-cause analysis (A–D).

2.5 | Statistical methods

This study was designed as a service evaluation so a priori power calculations were not undertaken. Pseudonymised data were managed using REDCap electronic data capture tools hosted at the Royal Devon and Exeter NHS Trust and statistical analyses were undertaken in R 3.6.1 (R Foundation for Statistical Computing).¹⁸ All analyses were two tailed and $P < 0.05$ were considered significant. We included patients with missing clinical data in analyses for which they had data and have specified the denominator for each variable. Descriptive statistics are reported as median and interquartile range for continuous variables and as number and proportions for categorical variables, unless otherwise stated.

The incidence of IBD-associated CRC was defined as the number of new cases of CRC occurring in patients with IBD. We report the mean incidence expressed per 100 000 persons per year between March 1998 and March 2019 and sought temporal changes in the incidence of CRC in patients with and without IBD using linear regression analyses. We report the number of patients who were adjudicated as having had a timely (A) or overdue (B) diagnosis, interval cancer (C) or missed opportunity for surveillance (D), as a proportion of the total number of patients eligible for surveillance. We matched patients with IBD-related CRC to CRC patients without IBD using the optimal method in the MatchIt package in R for sex, age at diagnosis, stage and location of cancer.¹⁹ Survival

rates were estimated using the Kaplan-Meier method and log-rank test.²⁰

2.6 | Ethical considerations and patient involvement

Patients were not involved in the conception or design of this study. In accordance with UK Health Research Authority guidelines, formal ethics approval was not mandated for this service evaluation.²¹

3 | RESULTS

3.1 | Overview

Among 4944 cases of colorectal adenocarcinoma diagnosed between March 1998 and March 2019: we identified 94 patients with a diagnosis of both IBD and CRC, representing 1.9% of all CRC treated at the Royal Devon and Exeter Hospital. Sixteen (16/94) of these cases were excluded as their IBD was diagnosed after their CRC, resulting in 78 cases of IBD-associated CRC. Patient disposition through the study is shown in (Figure 1).

The mean incidence of IBD-associated CRC in Devon from 1998 to 2019 was 165.4 per 100 000 patients with IBD (IQR 130.4–199.4) when adjusted for year-on-year changes in IBD prevalence.¹⁴ The mean incidence of sporadic CRC in Devon is 61.8 per 100 000 patients (IQR 57.6–67.5). Patients with IBD were at higher risk of developing CRC (odds ratio 2.7 [95% CI 1.6–3.9], $P < 0.001$). The incidence of CRC in patients with and without IBD has not changed significantly over the last 20 years (Figure 2).

3.2 | Baseline characteristics

Overall, 65% (51/78) patients with IBD-associated CRC were male with a median age of 69.7 years [61.0–78.0]. Most patients were white Europeans (97% [76/78]) and 35% (27/78) were current or ex-smokers. Seventy-two percent of patients (56/78) had UC, 22% (17/78) patients had Crohn's disease and 6% (5/78) inflammatory bowel disease unclassified (IBD-U). The median age at diagnosis of IBD was 46.4 years [IQR 31.9–62.1] with a median disease duration of 21.2 years [IQR 8.1–33.9]. Disease extent for UC and IBD-U, was limited to the rectum (E1) in 5% (4/78), left-sided (E2) in 26% (20/78) and extensive or pan-colitis (E3) in 40% (31/78) of patients. Crohn's disease was limited to the colon (L2) in 8% (6/78) and involved the ileum and colon (L3) in 10% (8/78) patients. Any family history of CRC was too poorly recorded to allow meaningful analysis. Three patients were diagnosed with primary sclerosing cholangitis. At the time of CRC diagnosis, 45% (35/78) patients were not being treated with any medications for their IBD; 41% (32/78) patients were treated with an aminosalicilate and/or immunosuppressant and one patient was treated with adalimumab (Table 1).

Cases of Colorectal Cancer in IBD patients at RDE March 1998 to March 2019

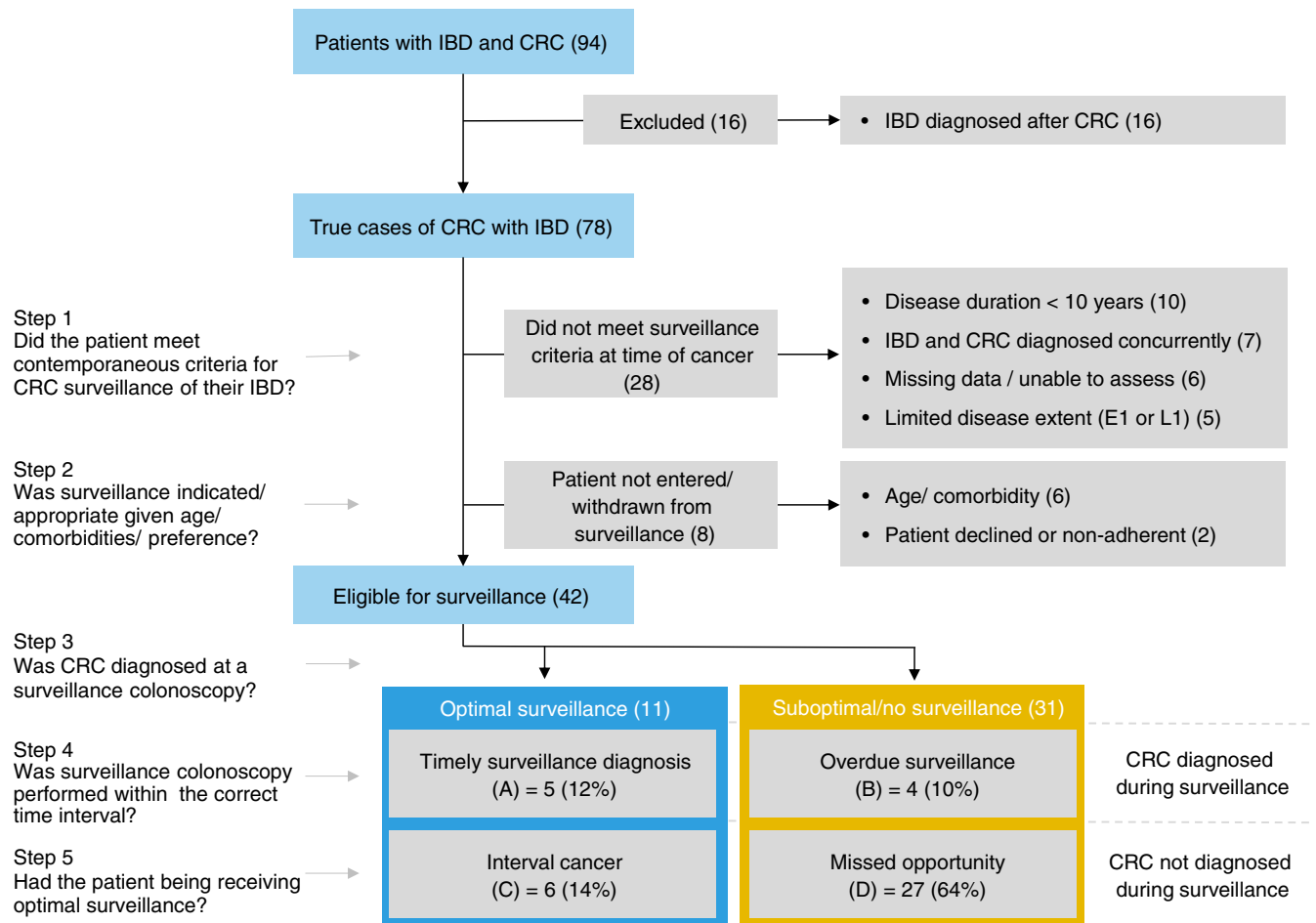


FIGURE 1 Patient flow diagram. IBD, inflammatory bowel disease; CRC, colorectal cancer; RDE, Royal Devon and Exeter Hospital; E1, Montreal Classification Extent 1 (ulcerative proctitis); L1, Montreal Classification Location 1 (terminal ileal).

At CRC diagnosis, 14% (11/78), 40% (31/78), 26% (20/78) and 20% (15/78) patients had Stage I, II, III and IV disease respectively. One patient did not have adequate staging data available. In total 39% (30/78) patients had rectal cancer, followed by 36% (28/78) with right-sided colon cancer, 21% (16/78) with sigmoid cancer and 4% (3/78) with descending colon cancer. Of the rectal cancers, 9% (7/78) of CRCs occurred in patients with retained rectums post subtotal colectomy for severe UC: 6% (5/78; 4 UC and 1 IBD-U) with an end ileostomy and rectal stump and 3% (2/78; 2 Crohn's disease) with an ileo-rectal anastomosis. In addition, there was one case where CRC occurred in the rectal stump of a patient with a defunctioning colostomy for perianal Crohn's disease.

3.3 | Root-cause analysis outcomes

At step 1, we removed 36% (28/78) patients because they did not meet contemporaneous criteria for CRC surveillance. Seven patients were diagnosed with IBD and CRC at the index colonoscopy.

Ten patients had had IBD for less than 10 years (median age at CRC diagnosis 70.2 years [IQR 71.1-78.2], disease duration of 4.3 years [IQR 2.3-5.6]). Five patients had proctitis (E1: $n = 3$) or ileitis (L1: $n = 2$) only, whose cancers occurred in areas of the colon that had not previously been affected by IBD. Six patients had too much missing data to allow us to determine if they met surveillance criteria or not.

At step 2, we removed 10% (8/78) patients: Six patients because of advanced age (median age 83.3 years [range 81.5-88.4]) and/or significant comorbidities (mean Charlson Comorbidity Index of 6.5 [IQR 6-7]) and two who had opted out of surveillance.

In the 42 patients eligible and suitable for surveillance: 12% (5/42) and 10% (4/42) patients were diagnosed with CRC at an appropriately timed (A) or overdue surveillance colonoscopy (B) respectively. Interval cancers (C) were observed in 14% (6/42) patients, 64% (27/42) patients had a missed opportunity (D) for colonoscopic surveillance (Figure 1).

Of the 42 patients eligible for surveillance, 6 (14%) patients had prior dysplasia. Four patients had intensified surveillance which led

Case rate of IBD-associated CRC (orange) corrected for IBD prevalence and sporadic CRC (black) corrected for Devon population over time

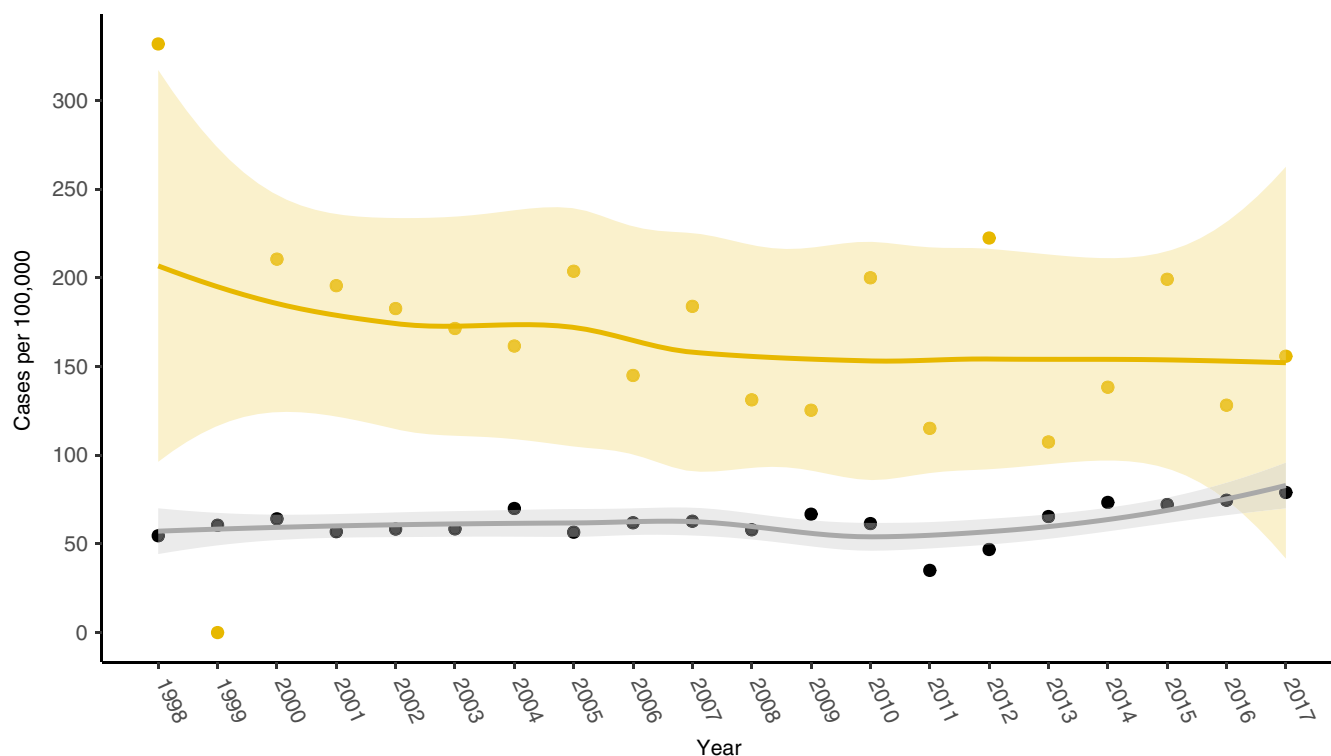


FIGURE 2 Incidence of IBD-associated and sporadic colorectal cancer (corrected for population changes year-on-year). CRC, colorectal cancer; IBD, inflammatory bowel disease.

to the timely detection of CRC. One patient was a missed opportunity due to failure to intensify surveillance for low grade dysplasia and the other was diagnosed at an overdue surveillance colonoscopy where a planned proctocolectomy for severe pan-colitis with dysplasia was delayed by the patient.

Of those patients with a missed opportunity for colonoscopic surveillance (D), 52% (14/27) were male, with a median age at CRC diagnosis of 64.9 years (IQR 60.4-74.3) and median disease duration of 24.8 years (IQR 15.4-32.4). Most patients (82% [22/27]) had UC: 45% (10/22) with extensive (E3) disease. Thirty seven percent (10/27) were current or ex-smokers. Only 11% (3/27) had previous surgeries for IBD. Eight cancers were located in the rectum, 10 in the sigmoid or descending colon and nine in the ascending colon. With regard to CRC stage at diagnosis, 15% (4/27), 44% (12/27), 22% (6/27) and 19% (5/27) had Stage 1, 2, 3 and 4 respectively. When the suboptimal surveillance group (overdue surveillance [B] and missed opportunity [D]) was compared with patients who had CRC detected by optimal surveillance (timely surveillance [A] and interval cancer groups [C]), the factors significantly associated with suboptimal surveillance were ulcerative colitis phenotype, older age at IBD diagnosis and the absence of resectional surgery (Table 2). Overall, 67% (17/27) of patients with a missed opportunity for surveillance were being managed in primary care leading up to their CRC diagnosis (Table 2, Table S1): Seven patients had been discharged back to primary care by either a gastroenterologist or surgeon without a plan for surveillance and

10 patients were unknown to secondary care. Of the patients with a missed opportunity, 37% (10/27) had not been offered surveillance despite on-going secondary care follow-up. In 15% (4/27) of patients, inadequacy of previous colonoscopies and/or failure to take into account previous histological findings contributed to delay in diagnosis of CRC.

3.4 | Case-control analysis to define survival outcomes of patients with IBD-associated CRC

We excluded 1/78 cases of IBD-associated colon cancer because missing staging data meant we were unable to perform matching. Between 1998 and 2019, 4850 patients without IBD were diagnosed with CRC in our catchment area. These patients were older at diagnosis (72.6 years [IQR 66.0-81.0] vs 67.3 years [IQR 60.9-77.9]) than patients with IBD-associated CRC, however, there were no significant differences in age at cancer diagnosis, sex, location, stage of CRC at diagnosis or survival (Table 3).

The Kaplan-Meier estimated probability of survival in IBD-associated CRC was 53.7% [90% CI 43.1-66.9] at 5 years and 38.5% [27.1-50.0] at 10 years (Figure 3). After matching for sex, age at diagnosis, stage and location of cancer, there were no differences in survival between patients with IBD-related or sporadic CRC (Figure 3) even in patients with a missed opportunity for surveillance (Figure S1).

TABLE 1 Baseline demographics of 78 included patients, stratified by eligibility for surveillance

	Total	Eligible for surveillance	Not eligible for surveillance	P
n (%) or median [IQR]	78	42	36	
Age at IBD diagnosis, y	46.4 [31.9-62.1]	36.9 [22.7-49.0]	58.0 [36.8-71.4]	<0.001
Age at CRC diagnosis, y	69.7 [61.0-78.0]	64.8 [58.7-73.3]	75.5 [66.9-81.5]	0.003
Sex				
Male	51 (65)	26 (62)	25 (69)	0.646
Female	27 (35)	16 (38)	11 (31)	
Ethnicity				
White	76 (97)	40 (95)	36 (100)	0.543
Asian	2 (3)	2 (5)	0 (0)	
Smoking history				
Never smoker	40 (51)	21 (50)	19 (53)	0.666
Current smoker	3 (4)	1 (2)	2 (6)	
Ex-smoker	24 (31)	15 (36)	9 (25)	
Not known	11 (14)	5 (12)	6 (17)	
IBD phenotype				
Ulcerative colitis	56 (72)	30 (71)	26 (72)	0.959
Crohn's disease	17 (22)	9 (21)	8 (22)	
IBD-U	5 (6)	3 (7)	2 (6)	
Montreal (A)				
A1	4 (5)	2 (5)	2 (6)	0.412
A2	30 (39)	19 (45)	11 (31)	
A3	44 (56)	21 (50)	23 (64)	
Montreal (E)—UC only				
E1	4 (5)	0 (0)	4 (11)	0.007
E2	20 (26)	16 (38)	4 (11)	
E3	31 (40)	17 (41)	14 (39)	
Montreal (L)—CD only				
L1	2 (3)	0 (0)	2 (6)	0.098
L2	6 (8)	3 (7)	3 (8)	
L3	8 (10)	6 (14)	2 (6)	
Duration of IBD to CRC diagnosis, y	46.4 [31.9-62.1]	24.8 [16.4-33.9]	5.9 [1.5-32.8]	0.002
Interval from last endoscopy to CRC diagnosis, y	2.3 [0-6.4]	4.3 [1.1-7.6]	2.7 [0.0-7.8]	0.256
Family history of CRC				
Yes	6 (8)	4 (10)	2 (6)	0.745
No	30 (39)	15 (36)	15 (42)	
Unknown	42 (54)	23 (55)	19 (53)	
Primary sclerosing cholangitis	3 (4)	3 (7)	0 (0)	0.096
At least one major comorbidity	36 (46)	19 (45)	17 (47)	1
Medication history				
None	35 (45)	13 (31)	22 (61)	n/a
Steroids	9 (12)	7 (17)	2 (6)	
5ASA only	27 (35)	12 (29)	15 (42)	
Thiopurine/methotrexate only	4 (5)	4 (10)	3 (8)	
Biologics	1 (1)	1 (2)	0 (0)	

(Continues)

TABLE 1 (Continued)

	Total	Eligible for surveillance	Not eligible for surveillance	P
Surgical history				
Subtotal colectomy and end ileostomy	5 (6)	4 (10)	1 (3)	0.454
Subtotal colectomy and anastomosis	2 (3)	2 (5)	0 (0)	
Defunctioning colostomy	1 (1)	1 (2)	0 (0)	

Abbreviations: 5ASA, 5-aminosalicylates; CD, Crohn's disease; CRC, colorectal cancer; IBD, inflammatory bowel disease; IBD-U, inflammatory bowel disease unclassified; IQR, interquartile range; Montreal (A), Montreal Classification Age; Montreal (E), Montreal Classification Extent; Montreal (L), Montreal Classification Location; UC, ulcerative colitis.

TABLE 2 Optimal surveillance vs suboptimal surveillance

	Optimal surveillance (A + C)	Suboptimal surveillance (B + D)	P
n	11	31	
Sex (%)			
Male	9 (82)	17 (55)	0.222
Female	2 (18)	14 (45)	
Smoking status (%)			
Never smoker	6 (55)	15 (48)	0.751
Current smoker	0 (0)	1 (3)	
Ex-smoker	3 (27)	12 (39)	
Not known	2 (18)	3 (10)	
IBD phenotype (%)			
Ulcerative colitis	4 (36)	26 (84)	0.01
Crohn's disease	5 (46)	4 (13)	
IBD-U	2 (18)	1 (3)	
Age at IBD diagnosis, years (median [IQR])	21.1 [19.4-34.6]	43.8 [30.4-49.3]	0.044
Primary sclerosing cholangitis (%)	1 (9)	3 (10)	1
Previous immunomodulator (%)	4 (36)	6 (19)	0.468
Previous biologic (%)	1 (9)	2 (7)	1
Previous bowel resection (%)	6 (55)	3 (10)	0.007
Age at CRC diagnosis, years (median [IQR])	62.3 [45.7-71.5]	66.4 [60.4-73.6]	0.271
CRC stage (%)			
1	0 (0)	6 (19)	n/a
2	6 (55)	13 (42)	
3	4 (36)	7 (23)	
4	1 (9)	5 (16)	
CRC location (%)			
Rectum	7 (64)	10 (32)	0.205
Rectosigmoid	0 (0)	6 (19)	
Right colon	3 (27)	11 (36)	
Sigmoid	0 (0)	3 (10)	
Descending colon	1 (9)	1 (3)	
Managed by (%)			
Secondary care	10 (64)	14 (36)	0.065
Primary care (GP)	1 (9)	17 (52)	

Abbreviations: CRC, colorectal cancer; GP, general practitioner; IBD, inflammatory bowel disease; IBD-U, inflammatory bowel disease unclassified; IQR, interquartile range.

TABLE 3 Demographics, stage and location of colorectal cancer in IBD, matched controls and sporadic controls

	IBD cases (n = 77) ^a	Matched controls (n = 307)	P	Unmatched controls (n = 4529)	P
Sex (male, %)	50 (65)	198 (64)	1.00	2282 (50)	0.047
Age at CRC diagnosis, years [median, IQR]	69.5 [61.0-78.0]	67.0 [59.1-75.0]	0.302	74.0 [66.0-81.0]	<0.001
Stage of CRC (%)					
1	11 (14)	21 (7)	0.093	489 (11)	0.536
2	31 (40)	133 (43)		1835 (41)	
3	20 (26)	68 (22)		1288 (28)	
4	15 (20)	86 (28)		915 (21)	
Location of CRC (%)					
Right colon	28 (36)	100 (33)	0.512	1605 (35)	0.121
Descending colon	3 (4)	20 (7)		241 (5)	
Other	0 (0)	0 (0)		175 (4)	
Rectum	30 (39)	105 (34)		1292 (29)	
Sigmoid	16 (21)	83 (27)		1227 (27)	
Survival [%; 95% CI]					
5-year	53.7 [43.1-66.9]	52.2 [46.9-58.1]	0.76	49.8 [48.4-51.3]	0.33
10-year	38.5 [27.1-50.0]	42.5 [37.3-48.4]		36.4 [34.8-38.0]	

Abbreviations: CI, confidence interval; CRC, colorectal cancer; IBD, inflammatory bowel disease; IQR, interquartile range.

^aOne IBD patient was excluded from matching based on missing staging data.

4 | DISCUSSION

4.1 | Key results and interpretation

Our patients with IBD are at increased risk of CRC, and irrespective of our current surveillance practice this has not changed over time (Figure 2). Overall, two-thirds of patients had a missed opportunity for surveillance. However, this delay in diagnosis did not influence stage of CRC at presentation or survival outcomes.

Based on our findings and those from another recent study that used primary care records to identify cases and thereby control for tertiary centre bias, the incidence of CRC in IBD appears to be static.^{14,22,23} It is contrary, however, to data from specialist endoscopy centres and from prospective population studies from Nordic countries that have reported falling CRC incidence rates.²⁴⁻²⁷ It is unclear why CRC rates have fallen in Denmark, Norway and Sweden but not the UK over a similar timeframe, since it is likely that all four countries have adopted similar treatment-targets: including the maintenance of remission with medical therapies, appropriately timed surgeries and the use of colorectal surveillance programmes.^{23,28-30} Static CRC rates amongst IBD patients in the UK may reflect poor integration between primary and secondary care services, impacting surveillance recall. In our cohort, for example, two-thirds of patients with a missed opportunity for CRC surveillance were being cared for exclusively by their general practitioner, nearly half of whom had been discharged by secondary care without a surveillance plan. Surveillance programmes without comprehensive recall systems are set to fail.

Our observation that one-third of IBD-associated CRCs were diagnosed in patients who were perceived to be at low-risk because of limited disease duration or extent, where surveillance had not started, is concerning. Whilst CRC is rarely encountered in the first few years of disease, early-onset IBD-related CRCs have been reported,³⁰ in particular in patients with concomitant primary sclerosing cholangitis.³¹ It may be that these patients had active IBD for many years prior to diagnosis. Even if we applied the most recent British Society of Gastroenterology guidelines⁶ that currently recommend commencing surveillance from eight years after diagnosis or onset of symptoms (if there was a significant delay before diagnosis) to all cases, only two additional patients would have been eligible for surveillance. Five sporadic CRCs were observed in segments of the colon previously unaffected by IBD. Whether more vigilance is required in patients who have isolated ileitis or proctitis who are reportedly not at increased risk of IBD is less clear. Adequate histological mapping to avoid underestimation of disease extent is clearly important, in particular, in patients phenotyped as having proctitis because they will not be enrolled in surveillance programs.³²⁻³⁵ Five patients developed CRC in their rectal stump after undergoing subtotal colectomies, hence it is important that these patients are also retained in a surveillance database.

Less clarity exists as to when to stop CRC surveillance. In our cohort, of the six patients who were deemed ineligible for surveillance due to their age and/or comorbidities, three underwent successful curative surgery. Arbitrary age cut-offs risk underuse of screening in healthy older patients. In IBD, individualised discussions taking into

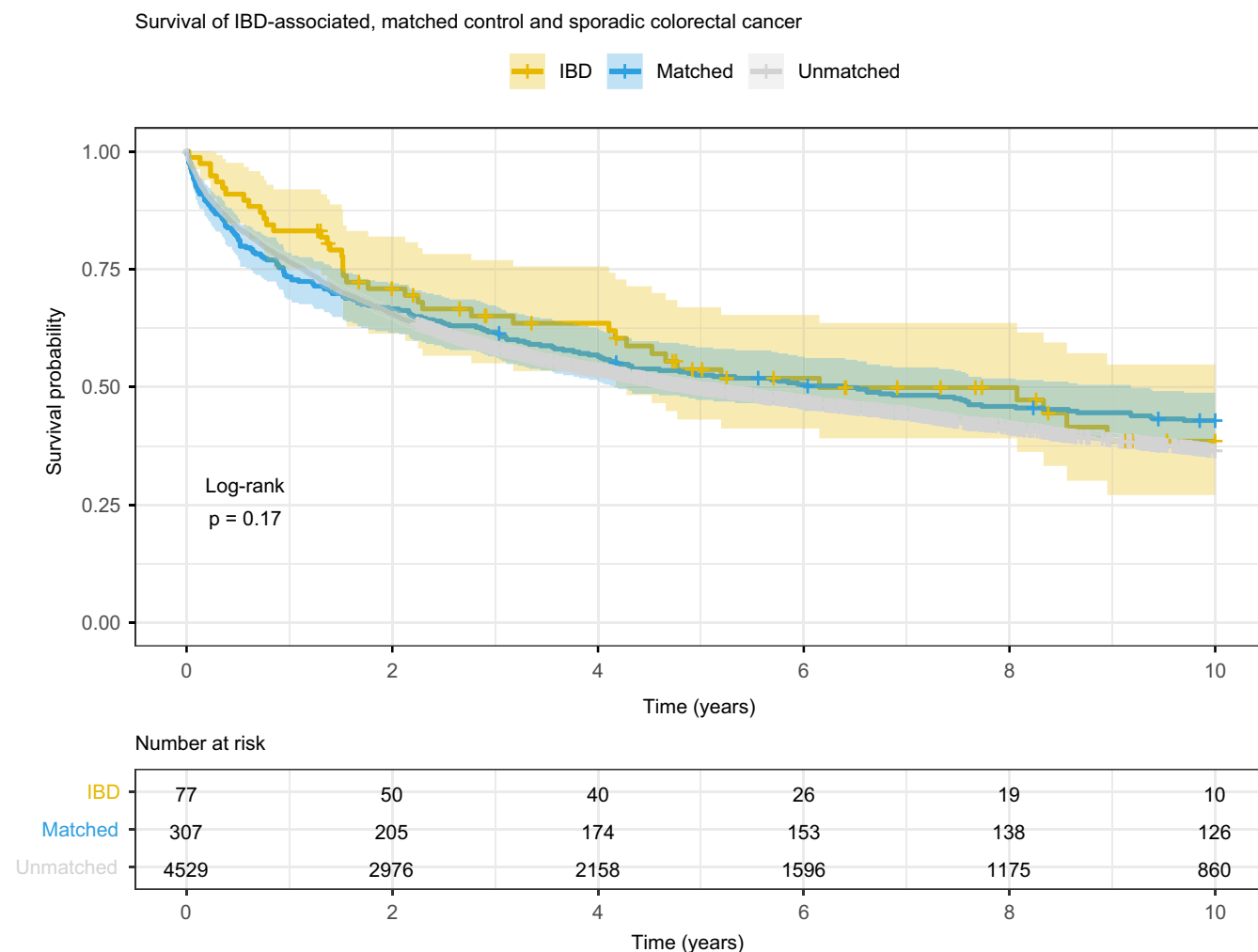


FIGURE 3 Colorectal cancer survival vs controls. CRC, colorectal cancer; IBD, inflammatory bowel disease

life expectancy as opposed to age, risk factors for IBD-associated CRC and consecutive negative findings at previous colonoscopies, seem appropriate.^{36,37}

4.2 | Limitations and generalisability

We acknowledge the following important limitations: first, we collected data from over 20 years and applied CRC surveillance guidelines in place at the time of cancer diagnosis: arguably, using a common set of guidelines would have decreased heterogeneity in data handling. Second, we relied on retrospective case note and database review and our data are limited by missingness and subject to interpretation bias. Third, our sample size, in particular, after excluding patients who were not eligible for surveillance was small and precluded subgroup analyses. Moreover, we were underpowered to detect the small differences in survival between patients with IBD-related and sporadic CRCs that have previously been observed. In this study, we excluded patients living outside our catchment area, so our results are likely to be generalisable to

non-tertiary centres in the UK. Whether other UK regions have similar proportions of patients managed exclusively in primary care has not been studied.

Accepting that the quality of the evidence is limited, with close concordance to surveillance guidelines, colonoscopic surveillance in IBD reduces the development of CRC and associated mortality through earlier detection and removal of pre-malignant lesion.^{22,27,38} Whilst artificial intelligence and non-invasive biomarkers of dysplasia are likely to increase the sensitivity of surveillance procedures, these newer techniques have not yet translated to routine clinical care.³⁹ In the meantime, we have designed a recall system embedded in our electronic record that prompts physicians when surveillance is due, and have completed a case finding survey in primary care.

5 | CONCLUSION

The incidence of IBD-associated colorectal has remained static. Two-thirds of patients eligible for colonoscopic surveillance had a missed opportunity to diagnose CRC. Surveillance programmes

without comprehensive and fully integrated recall systems across primary and secondary care are set to fail.

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AUTHORSHIP

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SUPPORTING INFORMATION

Additional supporting information will be found online in the Supporting Information section.

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